Remarks

Claims 53, 55 – 58 and 61 - 64 are active in the case. Claims 53 is the only independent claim. The present invention relates to an improved method for treating osteoporosis with an effervescent bisphosphonate solution having high buffering capacity, combined with an anti-ulcer agent.

The Rejection of Claims under 35 U.S.C. § 103

Claims 53 – 64 stand rejected under 35 U.S.C. § 103 as being obvious over Katdare et al. (US 5,853,759) in view of Daifotis (U.S. 5,994,329). Applicants submit herewith the Hayward Declaration and agurments filed in co-pending application 10/273,081 to supplement the record of this case. The Examiner may believe that since the dose of alendronate in Katdare is 5-10 mg, while that of the present invention is 50 – 120 mg, a person of ordinary skill in the art would have increased the amount of buffering components and other excipients automatically once it was decided to increase the dose of alendronate. However, as explained in the Hayward Declaration submitted herewith, that assumption is not correct.(Decl. ¶ 4 -10)

Effervescent pharmaceutical formulations are typically designed to be dissolved in 100 to 200 ml of water regardless of the dosing strength, with the volume largely dependent upon the nature of the active ingredients (drug, vitamin, mineral, or other nutritional product) and the commercial objective. The effervescent form itself simply provides a means of dispersing the drug into water solution for easy consumption, particularly for drugs where there is a large dosage.

If the ingredients do not have a bad taste, the volume of the dosing solution is routinely kept to 50-100 ml or so. This volume of reconstitution is independent of the drug dose, so that in the case of ingredients where flavor is not an issue, the only variable is the amount of active ingredient in the tablet. That is the case with products such as vitamin C, where doses of 60 mg to 1000 mg are also delivered in a single tablet at a maximum volume of 200 ml (3 to 6 ounces or so).

Alendronate has no taste and is readily soluble in water. Therefore, if the alendronate dose were raised from the very small 5 to 10 mg doses of Katdare, up to 70 mg or even more, there would be no logical basis to increase the amount of the effervescent couple or the excipients. To the contrary, from the standpoint of cost the smallest tablet that generates an effective solution for consumption would be selected. So a dosing volume of 100 to 200 ml would probably not be increased at all and certainly not by a factor of 7 when increasing the dose of alendronate from 10 mg to 70 mg, because that would result in a dosing volume of 700 to 1400 ml, which is a prohibitive volume for dosing. The Katdare examples are typical of effervescent formulations that are palatable for alendronate, independent of the dose and deliverable in a reasonable (100-200 ml volume). In contrast, the present formulation was developed in order to control the pH of the stomach over time and the dosage of alendronate does not affect the amount of buffering capacity needed to achieve the desired results.

Conclusions

Applicants submit that the case is now in condition for allowance. Early notice to that effect is earnestly requested.

If it is deemed helpful or beneficial to the efficient prosecution of the present application, the Examiner is invited to contact Applicant's undersigned representative by telephone.

Respectfully submitted,

/RobertHahl#33,893/

Robert W. Hahl, Ph.D.
Reg. No. 33,893

Neifeld IP Law, PC
4813-B Eisenhower Avenue
Alexandria, VA 22304
Tel: 703-415-0012 ext. 25
Fax: 703-415-0013